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EXAMINER

BROWN, TIMOTHY M

ART UNIT PAPER NUMBER

1648

DATE MAILED: 11/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/044,955

Applicant(s)

ROBERTS ET AL.

Examiner

Tim Brown

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 August 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-127 is/are pending in the application.
- 4a) Of the above claim(s) 1-77 and 81-127 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 78-80 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>4/13/04 et seq.</u> | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

This non-final Office action is responsive to the communication received August 9, 2004.

Claims 1-127 are pending. Claims 1-77 and 81-127 are withdrawn. Claims 78-80 are under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 78-80 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention without undue experimentation.

Courts consider a number of factors when determining whether undue experimentation is required to make and use a claimed invention. These factors include the following: the breadth of the claims; the nature of the invention; the state of the prior art; the level of one of ordinary skill; the level of predictability in the art; the amount of direction provided by the inventor; the existence of working examples; and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404.

Applicants claim a method for identifying a virus with antineoplastic activity in a mammal, comprising using a test virus to infect i) cells deficient in an interferon-mediated antiviral activity, and ii) cells competent in an interferon-mediated antiviral activity, and determining whether the virus preferentially kills the cells that are deficient in the interferon-mediated antiviral activity as compared to the cells that are competent in interferon-mediated antiviral activity, wherein the cells are human head and neck carcinoma cells.

Turning to the *Wands* factors, Applicants' invention is broadly claimed as a screening assay for identifying a virus that has antineoplastic activity in a mammal. The invention identifies *any* virus that preferentially kills interferon-deficient cells as having antineoplastic activity in a mammal.

Although a large number of antineoplastic viruses have been identified, the art has not witnessed a simple screening assay for identifying a virus that has antineoplastic activity in a mammal. This is due to the lack of predictability in identifying viruses that have oncolytic activity in *in vitro* models and animal models.

Although *in vitro* models are useful for selecting viruses for further study, they do not necessarily indicate how a virus will behave *in vivo*. One factor that cell models cannot duplicate is the mammalian immune system. Viruses that have shown promise in cell models have gone on to be irradiated by the immune response when administered for antitumor therapy in a mammal (Mullen, J.T. *The Oncologist* (2002); 7, 106-119, 109). Another factor that impacts whether a virus will have antineoplastic activity in a mammal is the virus' phenotype. Many viruses that are oncolytic *in vitro* require adaptation before they can preferentially infect and kill tumor cells in a mammal (Sinkovics, J. *Intervirology* (1993); 36, 193-214, 199). These factors

combine to make identifying viruses that have antineoplastic activity in a mammal an unpredictable art.

Because of this unpredictability, one skilled in the art would have to rely heavily on Applicants' specification in order to practice the invention. The specification, however, fails to provide adequate direction for practicing the claimed invention. This is because the content of Applicants' specification relates to purifying viruses for compounds, and using the compounds for the treatment of neoplasms; the specification is silent on a screening assay for identifying a virus that has antineoplastic activity in a mammal. Applicants' specification also lacks working examples. The examples cited by Applicants do not demonstrate that cells with different levels of interferon expression can be used to identify an antineoplastic virus. Rather, Applicants' examples only show that the virus PPMK107 preferentially kills human tumor cells *in vitro* and in mice. Applicants' specification therefore fails to provide adequate direction for practicing the claimed invention.

Based on the foregoing factors, *In re Wands* requires a finding that the specification does not allow one skilled in the art to practice the claimed invention without undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 78-80 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 78-80 are indefinite for the following reasons.

First, claim 78 recites "[a] method for identifying a virus with antineoplastic activity in a mammal comprising . . . using said virus to infect cells" It is unclear how infecting cells

with a virus that has been identified as neoplastic, can identify that virus as antineoplastic. In other words, it is unclear how Applicants' method identifies an antineoplastic virus, when it begins with an antineoplastic virus in the first place.

Second, claims 78-80 are indefinite for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Claim 78 is drawn to a method of identifying a virus having antineoplastic activity in a mammal comprising, using a test virus to infect (1) cells deficient in interferon-mediated antiviral activity, and (2) competent in interferon-mediated antiviral activity, and determining whether the test virus preferentially kills the cells deficient in interferon-mediated antiviral activity. The step that is omitted from claim 78 is identifying the virus as antineoplastic based on the method's determining step. Simply observing (i.e. determining) that a test virus preferentially kills interferon deficient cells does not identify the virus as antineoplastic. Identifying the virus as antineoplastic requires a step wherein observing that a test virus preferentially infects the deficient cells is correlated with antineoplastic activity.

Third, claims 78-80 are indefinite in that the use of "preferentially" is an impermissible term of degree. This term renders the claims indefinite for the reasons stated in this Office action and the previous Office action.

Fourth, claims 78-80 are indefinite for reciting "a virus with antineoplastic activity." The term "Antineoplastic" denotes that the virus is capable of killing a neoplasm (i.e. tumor cell). Since a virus may kill a tumor cell through reproductive lysis, inducing the expression of cytotoxic proteins, or inducing nonspecific anti-tumor immunity (Mullen, J.T. The Oncologist (2002); 7, 106-119, 107), the term "antineoplastic" refers to several different viral activities. Therefore, one skilled in the art would not know what types of viral activity are covered by the

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claims. The claims are therefore indefinite for failing to clarify the scope of Applicants' invention.

Claims 78-80 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. As noted above, Applicants' specification discloses purifying viruses for compounds, and using the compounds for the treatment of neoplasms. The specification lacks any disclosure of a method of screening for antineoplastic viruses comprising using a virus to infect interferon-deficient cells, and interferon-competent cells, and determining whether the virus preferentially kills the interferon-deficient cells. The specification similarly lacks working examples of such a method. Therefore, the specification fails to establish that Applicants were in possession of the claimed invention at the time the application was filed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 78-80 are rejected under 35 U.S.C. 102(b) as being anticipated by Reichard

(Reichard K.W. Journ. Surg. Res. (1992) ; 52, 448-453).

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Although Applicants' invention is drawn to a method for identifying a virus with antineoplastic activity in a mammal, the invention only performs two steps. That is, the invention 1) uses a virus to infect cells i) deficient in an interferon-mediated antiviral activity, and ii) competent in an interferon-mediated antiviral activity, and 2) determines whether the virus preferentially kills the cells deficient in an interferon-mediated antiviral activity.

Reichard inherently teaches Applicants' step of using a test virus to infect interferon deficient cells and interferon competent cells. This follows from Reichard's disclosure of using Newcastle disease virus to infect normal human fibroblasts, and several different human tumor cell lines (see abstract). As noted in Applicants' specification at page 16, tumor cells are deficient in interferon-mediated antiviral activity when compared to normal cells. Thus, Reichard's disclosure of infecting normal cells and tumor anticipates the infecting of interferon-deficient cells and interferon-competent cells as claimed by Applicants.

Note that the limitation "using said virus to infect" has been interpreted as 'using a test virus to infect.' This was done to facilitate an examination of the claims on their merits.

Response to Arguments

The Examiner notes with appreciation that Applicants have submitted copies of the references requested in the previous Office action. These references have been considered as noted in the PTO-1449 attached to this Office action. The rejection of claim 78 under 35 U.S.C. 103(a) is withdrawn in view of Applicants' remarks. The rejection of claims 78-80 under 35 U.S.C. 112, second paragraph is maintained.

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Claims 78-80 were rejected as indefinite because the term “preferentially” was identified as an impermissible term of degree. Applicant argues this rejection should be withdrawn in view of their amendment and remarks. Claim 78 was amended to recite “preferentially as compared to.” Applicants note that the invention “is a comparative method in which the standard for measuring the degree of preferential killing is at the heart of the invention.” The Examiner respectfully submits Applicants’ have not overcome the rejection of the claims. The fact that the method is a comparative one does not provide clarity to “preferentially.” Does the virus kill interferon-deficient cells preferentially if it kills a simple majority of interferon-deficient cells? Or, does the virus have to kill 10% more interferon deficient cells than interferon-competent cells in order for the killing to be labeled “preferential.” The specification does not provide any clarity as to the meaning of “preferentially.” Therefore, one skilled in the art would not be able to ascertain the scope of the claimed invention.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy M. Brown whose telephone number is (571) 272-0773. The examiner can normally be reached on Monday - Friday, 8am - 5pm.

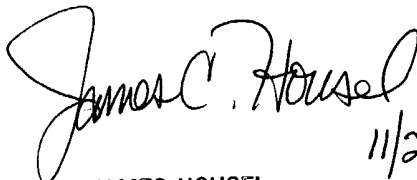
If attempts to reach the examiner by telephone are unsuccessful, the examiner’s supervisor, James Housel can be reached on (571) 272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Timothy M. Brown
Examiner
Art Unit 1648

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11/29/04
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